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PTO/SB/05 (4/98)

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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 C.F.R. § 1.53(b))

Attorney Docket No. ALBIHN W 3.3-258 CONT

First Inventor or Application Identifier Lennart Cedgård

Title METHOD FOR THE PRODUCTION OF TABLETS BY
PRESSING AND TABLETS PRODUCED BY THE METHOD

Express Mail Label No

EM411073469US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

ADDRESS TO: Box Patent Application
Washington, DC 20231

1. ☒ * Fee Transmittal Form (e.g., PTO/SB/17)
(Submit an original and a duplicate for fee processing)
2. ☒ Specification [Total Pages 9]
(preferred arrangement set forth below)
 - Descriptive title of the invention
 - Cross References to Related Applications
 - Statement Regarding Fed sponsored R & D
 - Reference to Microfiche Appendix
 - Background of the invention
 - Brief Summary of the invention
 - Brief Description of the Drawings (if filed)
 - Detailed Description
 - Claim(s)
 - Abstract of the Disclosure
3. ☐ Drawing(s) (35 U.S.C. 113) [Total Sheets]
4. Oath or Declaration [Total Pages 2]
 - a. ☐ Newly executed (original or copy)
 - b. ☒ Copy from a prior application (37 C.F.R. § 1.63(d))
(for continuation/divisional with Box 16 completed)
 - i. ☐ DELETION OF INVENTOR(S)
Signed statement attached deleting
inventor(s) named in the prior application,
see 37 C.F.R. §§ 1.63(d)(2) and 1.33(b).

5. ☐ Microfiche Computer Program (Appendix)
6. Nucleotide and/or Amino Acid Sequence Submission
(if applicable, all necessary)
 - a. ☐ Computer Readable Copy
 - b. ☐ Paper Copy (identical to computer copy)
 - c. ☐ Statement verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

7. ☐ Assignment Papers (cover sheet & document(s))
8. ☐ 37 C.F.R. § 3.73(b) Statement of Power of Attorney
(when there is an assignee)
9. ☐ English Translation Document (if applicable)
10. ☐ Information Disclosure Statement (IDS)/PTO-1449 [Copies of IDS Citations]
11. ☐ Preliminary Amendment
12. ☒ Return Receipt Postcard (MPEP 503)
(Should be specifically itemized)
13. ☐ * Small Entity Statement(s) [Statement filed in prior application, Status still proper and desired (PTO/SB/09-12)]
14. ☐ Certified Copy of Priority Document(s)
(if foreign priority is claimed)
15. ☒ Other: Three Month Extension
Petition

NOTE FOR ITEMS 1 & 13: IN ORDER TO BE ENTITLED TO PAY SMALL ENTITY
FEES, A SMALL ENTITY STATEMENT IS REQUIRED (37 C.F.R. § 1.27), EXCEPT
IF ONE FILED IN A PRIOR APPLICATION IS RELIED UPON (37 C.F.R. § 1.28).

16. If a CONTINUING APPLICATION, check appropriate box, and supply the requisite information below and in a preliminary amendment:

☒ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application No: 09 / 029336

Prior application information: Examiner Afremova

Group / Art Unit: 1651

For CONTINUATION or DIVISIONAL only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 4b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation can only be relied upon when a portion has been inadvertently omitted from the submitted application parts.

17. CORRESPONDENCE ADDRESS

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Name (Print/Type)	Arnold H. Krumholz	Registration No. (Attorney/Agent)	25,428
Signature	[Signature]		Date 12/17/99

Burden Hour Statement. This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231.

5 TITLE: Method for the production of tablets by pressing and
tablets produced by the method.

TECHNICAL FIELD:

10 The present invention relates to a method for the
production of tablets by pressing of tablet material which
contains microorganisms.

PRIOR ART:

15 Tablets are usually produced by pressing of a pulverulent
tablet mass in a suitable shape in a so-called tablet
punching machine. The tablets may have different shape and
be of different size and they may also be of different
hardness dependent on the properties of the tablet mass and
20 the pressure to which they are subjected during the
punching of the tablets.

25 When the tablets are formed heat is developed as a result
of the friction against the mould surfaces and the inner
friction in the tablet mass. Since the tablets usually
consist of chemicals and the temperature increase is not
too high, this will not create any problem since the
chemicals can resist this heat increase and also are cooled
rapidly. However, some tablet masses contain living
microorganisms, such as bacteria, which are sensitive to
30 high temperatures and because of this some of these
bacteria die during the tablet punching.

TECHNICAL PROBLEM:

35 Tablets which contain microorganisms, for instance in the
form of bacteria, and which are intended to contain such
organisms will lose a part of or all of their value when
the microorganisms are destroyed during the tablet
punching. This cannot be avoided by simply using a lower
pressure on the conventional tablet mass and thereby
40 creating a lower heat development since the tablet must be

subjected to a certain pressure so that it maintains its shape and is not crumbled. For known tablet masses it is not unusual that a reduction of the viability (survival) of the bacteria in the tablet is up to 80% and even more.

5

SOLUTION:

It has therefore always been a problem to be able to produce tablets which contain microorganisms in the form of bacteria with a lesser reduction of the viability from tablet mass to a complete tablet and therefore according to the invention a method has been obtained for the production of tablets by pressing of tablet material comprising living organisms, which is characterized in that the tablet material also contains oligosaccharides consisting of more than two monosaccharides.

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According to the invention, it is suitable that the oligosaccharides consist of fructose oligosaccharides, preferably inulin.

20

According to the invention it is suitable that the oligosaccharides are present in an amount of 40-99.5 % by weight of the tablet material.

25

The tablet material according to the invention can suitably contain microorganisms consisting of lactic acid producing bacteria.

30

The invention also comprises tablets produced by the method according to the invention, which tablets contain oligosaccharides and microorganisms whereby the oligosaccharides suitably consist of fructose oligosaccharides, preferably inulin.

35

The tablets according to the invention may contain lactic acid producing bacteria as microorganisms and they may also

contain other additives such as polysaccharides, for example microcrystalline cellulose and starch, as well as other additives such as calcium diphosphate.

5 DETAILED DESCRIPTION:

10 The tablets according to the invention comprise microorganisms, preferably lactic acid producing bacteria cultures known as probiotica, which are intended to normalise or balance bacterial flora being present in the stomach and the intestine of humans or animals, but they may also contain other types of bacteria.

15 By mixing oligosaccharides, preferably fructose oligosaccharides, in the tablet mass as a so-called supporting substance the tablet punching is facilitated, which makes it possible to punch tablets at a lower pressure and lower heat development at the same time as the hardness of the tablet is maintained. The brittleness of the tablet, the friability, is surprisingly not changed with the tablet mass according to the present invention.

20 Due to this new composition, the punching pressure for the tablet making maybe reduced by up to 50% compared to conventional tablet punching methods without any reduction of the friability. This friability according to the invention will be 0.3-0.5, which is to be compared with the reference values which are accepted according to GMP (Good Manufacturing Practice) which are within the range of 0.1-1.0. The friability is expressed in percent weight reduction of the tablets when they are rotated 100 revolutions in a standard testing machine.

25 The amount of oligosaccharides depends on different crystalline qualities but may suitably be 99.5-40 weight percent of the total tablet mass without admixing any other supporting substance. However, if desired, known supporting

30

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substances such as calcium diphosphate, microcrystalline cellulose and starch may be added in a suitable small amount. A smaller addition of oligosaccharides can, however, give rise to a smaller difference with regard to the viability compared with tablet masses containing only conventional supporting substances.

The tablets according to the present invention have a lower hardness due to the lower punching pressure when the tablets are formed but an increased viability for the strain of bacteria, which makes every tablet more efficient than conventional tablets. By not pressing the tablets so hard the yield of tablets for a given amount of tablet mass will also increase.

The invention will be described more in detail below by means of two examples, of which Example 1 describes a method according to the present invention and Example 2 describes a method of conventional kind.

Example 1: recipe having an active substance and tablet filling material

Str. thermophilus & L. bulgaricus	50%
Bifidobacterium animalis	0.5%
L. plantaris	0.5%
Inulin (fructose oligosaccharides)	<u>49%</u>
	<u>100%</u>

Hardness: 2.75 kp Friability: 0.3
Viability original granulate: 5E8 cfu/g
Viability tablet: 3E8 cfu/g
40% reduction of cfu (colony forming units)

Example 2: recipe having active substance and tablet filling material

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Str. thermophilus & L. bulgaricus	50%
Bifidobacterium animalis	0.5%
L. plantaris	0.5%

5	Calcium diphosphate	20%
	Microcrystalline cellulose	18%
	Starch	<u>11%</u>
		100%

10 Hardness: 5.5 kp Friability: 0.3%
 Viability original granulate: 5E8 cfu/g
 Viability tablet: 1E8 cfu/g
 80% reduction of cfu (colony forming units)

15 As appears from the above examples, the friability is
 maintained unchanged with a value of 0.3 whereas the
 hardness has been decreased to 2.75 kp compared with 5.5 kp
 for the conventional method. The viability has increased
20 from 1E8 cfu/g to 3E8 cfu/g according to the invention. The
 reduction of cfu from tablet mass to tablet during the
 tablet punching became only 40% according to the new method
 and 80% according to the conventional method.

25 Accordingly, the new method results in an increased
 maintained viability after tablet punching of up to 200%
 compared with conventional tablet fillers. The increased
 yield results in an appreciably better economy and quality
 improvement of the above products.

30 The invention is not limited to the embodiments shown above
 but can be varied in different ways within the scope of the
 claims.

5 CLAIMS:

1. Method for the production of tablets having high
viability in the tablet by pressing tablet material
containing living microorganisms,
10 c h a r a c t e r i z e d i n t h a t t h e t a b l e t m a t e r i a l
also contains oligosaccharides.

2. Method according to claim 1
c h a r a c t e r i z e d i n t h a t t h e o l i g o s a c c h a r i d e s
15 are present in an amount of 40-99.5 percent by weight of
the tablet material.

3. Method according to any of claims 1-2,
c h a r a c t e r i z e d i n t h a t t h e o l i g o s a c c h a r i d e s
20 consist of fructose oligosaccharides.

4. Method according to any of claims 1-3,
c h a r a c t e r i z e d i n t h a t t h e o l i g o s a c c h a r i d e s
25 consist of inulin.

5. Method according to any of claims 1-4,
c h a r a c t e r i z e d i n t h a t t h e m i c r o o r g a n i s m s
consist of lactic acid producing bacteria.

6. Tablets produced according to any of claims 1-5
30 containing oligosaccharides and microorganisms.

7. Tablets according to claim 6,
c h a r a c t e r i z e d i n t h a t t h e o l i g o s a c c h a r i d e s
35 consist of fructose oligosaccharides.

8. Tablets according to any of claims 6-7,
c h a r a c t e r i z e d i n t h a t t h e o l i g o s a c c h a r i d e s
40 consist of inulin.

9. Tablets according to any of claims 6-8,
c h a r a c t e r i z e d i n t h a t t h e m i c r o o r g a n i s m s
consist of lactic acid producing bacteria.

5 10. Tablets according to any of claims 6-9,
c h a r a c t e r i z e d i n t h a t t h e y a l s o c o n t a i n
polysaccharides such as microcrystalline cellulose and
starch as well as other additives such as calcium
diphosphate.

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AMENDED CLAIMS

[received by the International Bureau on 24 December 1996 (24.12.96);
original claims 1 - 10 replaced by amended claims 1 - 10 (2 pages)]

1. Method for the production of tablets having high
viability in the tablet by pressing tablet material
containing living microorganisms,
c h a r a c t e r i z e d i n that the tablet material
also contains oligosaccharides consisting of more than two
monosaccharides.

2. Method according to claim 1
c h a r a c t e r i z e d i n that the oligosaccharides
are present in an amount of 40-99.5 percent by weight of
the tablet material.

3. Method according to any of claims 1-2,
c h a r a c t e r i z e d i n that the oligosaccharides
consist of fructose oligosaccharides.

4. Method according to any of claims 1-3,
c h a r a c t e r i z e d i n that the oligosaccharides
consist of inulin.

5. Method according to any of claims 1-4,
c h a r a c t e r i z e d i n that the microorganisms
consist of lactic acid producing bacteria.

6. Tablets produced according to any of claims 1-5
containing oligosaccharides and microorganisms.

7. Tablets according to claim 6,
c h a r a c t e r i z e d i n that the oligosaccharides
consist of fructose oligosaccharides.

8. Tablets according to any of claims 6-7,
c h a r a c t e r i z e d i n that the oligosaccharides
consist of inulin.

AMENDED SHEET (ARTICLE 19)

10. Tablets according to any of claims 6-9, characterized in that they also contain polysaccharides such as microcrystalline cellulose and starch as well as other additives such as calcium diphosphate.

AMENDED SHEET (ARTICLE 19)

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

ATTORNEY'S DOCKET NO.: ALBIHN W 3.3-258

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: "Method for the production of tablets by pressing and tablets produced by the, the specification of which method"

☐ is attached hereto

☒ was filed on 23.08.96

Number PCT/SE96/01043 as United States Application Number or PCT International Application and was amended on 24.12.96 (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATION(S)			
COUNTRY	APPLICATION NUMBER	DATE OF FILING (month, day, year)	PRIORITY CLAIMED
Sweden	9502941-9	08-25-95	YES <input checked="" type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>

LISTING OF FOREIGN APPLICATIONS CONTINUED ON PAGE 3 HEREOF ☐ YES ☒ NO

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below:

Application Number: _____ Filing Date: _____

Application Number: _____ Filing Date: _____

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

U.S. Parent Application Serial Number: _____ Parent Filing Date: _____ Parent Patent No.: _____

U.S. Parent Application Serial Number: _____ Parent Filing Date: _____ Parent Patent No.: _____

PCT Parent Number: _____ Parent Filing Date: _____

LISTING OF US APPLICATIONS CONTINUED ON PAGE 3 HEREOF: ☐ YES ☒ NO

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

Lawrence I. Lerner, Reg. No. 19,516, Sidney David, Reg. No. 22,768, Joseph S. Littenberg, Reg. No. 20,832, Arnold H. Krumholz, Reg. No. 25,428, William L. Mentlik, Reg. No. 27,108, John R. Nelson, Reg. No. 26,573, Roy H. Wegner, Reg. No. 28,350, Stephen B. Goldman, Reg. No. 28,512, Paul H. Kochanski, Reg. No. 29,660, Marcus J. Millet, Reg. No. 28,241, Bruce H. Sales, Reg. No. 32,793, Daniel H. Bobis, Reg. No. 16,694, Peter J. Butch III, Reg. No. 32,203, Kerth E. Gilman, Reg. No. 32,137, Robert B. Cohen, Reg. No. 32,768, Arnold B. Dompier, Reg. No. 29,736, Michael H. Teschner, Reg. No. 32,862, Jeffrey S. Dickey, Reg. No. 35,858, Gregory S. Gewirtz, Reg. No. 36,522, Jonathan A. David, Reg. No. 36,494, Shawn P. Foley, Reg. No. 33,071, Robert T. Canavan, Reg. No. 37,592

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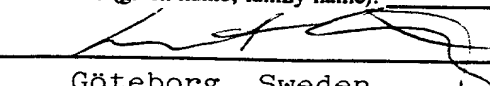
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(name and telephone number)
Arnold H. Krumholz
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DECLARATION - Page 2

ATTORNEY DOCKET NO. ALBIHN W 3.3-258

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor (given name, family name): Lennart Cedgård

Inventor's signature  Date February 16, 1998

Residence: Göteborg, Sweden Citizenship: Sweden

Post Office Address: Skolgatan 26, S-413 02 Göteborg, Sweden

Full name of second joint inventor, if any (given name, family name):

Second Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of third joint inventor, if any (given name, family name):

Third Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of fourth joint inventor, if any (given name, family name):

Fourth Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of fifth joint inventor (given name, family name):

Fifth Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of sixth joint inventor, if any (given name, family name):

Sixth Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of seventh joint inventor, if any (given name, family name):

Seventh Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of eighth joint inventor, if any (given name, family name):

Eighth Inventor's signature _____ Date _____

Residence: _____ Citizenship: _____

Post Office Address: _____

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of :
Lennart Cedgård :
 : Group Art Unit: 1651
A Continuation of :
U.S. Application No. 09/029,336 :
 : Examiner: V. Afremova
Filing Date: Herewith :
 :
For: METHOD FOR THE PRODUCTION OF : Date: December 17, 1999
TABLETS BY PRESSING AND TABLETS :
PRODUCED BY THE METHOD :
 :
 : X

Assistant Commissioner for Patents
Washington, D.C. 20231

EXTENSION PETITION

Sir:

The undersigned attorney respectfully petitions for a three-month extension of time to reset the deadline for response to the Office Action in the above-identified application from September 17, 1999 to and including December 17, 1999. Applicant's Continuing Application is enclosed herewith.

Please charge Deposit Account No. 12-1095 in the amount of \$870.00.

In the event the actual fee is greater than the amount above, the Patent Office is authorized to charge any deficiency to our Deposit Account No. 12-1095.

Respectfully submitted,

LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK, LLP



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